

Claims

- Sub C¹
1. ~~Pharmaceutical composition comprising as an active agent an immunologically protective living vaccine which is a recombinant attenuated microbial pathogen, which comprises at least one heterologous nucleic acid molecule encoding a Helicobacter antigen, wherein said pathogen is capable of expressing said nucleic acid molecule or capable of causing the expression of said nucleic acid molecule in a target cell.~~
 2. ~~The composition according to claim 1, wherein the pathogen is an enterobacterial cell, especially a Salmonella cell.~~
 3. ~~The composition according to claim 1 or 2, wherein the pathogen is a Salmonella aro mutant cell.~~
 4. ~~The composition according to any of claims 1-3, wherein the Helicobacter ^{immunogen} antigen is urease, a urease subunit, an immunologically reactive fragment thereof, or a peptide mimotope thereof.~~ ^{claim 1}
 5. ~~The composition according to any one of claims 1-3, wherein the Helicobacter ^{immunogen} antigen is a secretory polypeptide from Helicobacter, an immunologically reactive fragment thereof, or a peptide mimotope thereof.~~ ^{claim 1}
 - ~~The composition according to any one of claims 1-3 and 5, wherein the Helicobacter antigen is selected from the group consisting of the antigens AlpA, AlpB, immunologically reactive fragments thereof, or a peptide mimotope thereof.~~ ^{claim 1}
 7. ~~The composition according to any one of claims 1-6, wherein said nucleic acid molecule encoding a Helicobacter ^{immunogen} antigen is capable to be expressed phase variably.~~ ^{claim 1}
 8. The composition according to claim 7,
- Sub E³
- Sub E³

C wherein said nucleic acid molecule encoding the Helicobacter ^{immunogen} antigen is under control of an expression signal which is substantially inactive in the pathogen and which is capable to be activated by a nucleic acid reorganization caused by a nucleic acid reorganization mechanism in the pathogen.

9. The composition according to claim 8, wherein the expression signal is a bacteriophage promoter, and the activation is caused by a DNA reorganization resulting in the production of a corresponding bacteriophage RNA polymerase in the pathogen.

10. The composition according to ^{claim 1} ~~any one of claims 1-9~~, wherein said pathogen further comprises at least one second nucleic acid molecule encoding an immunomodulatory polypeptide, wherein said pathogen is capable to express said second nucleic acid molecule.

11. The composition ^{claim 1} ~~claims 1-10~~, according to ~~any one of~~ together with pharmaceutically acceptable diluents, carriers and adjuvants.

12. The composition according to claim 11, which is suitable for administration to a mucosal surface or via the parenteral route.

13. A method for the preparation of a living vaccine comprising formulating a pharmaceutical composition according to ^{claim 1} ~~any one of claims 1-10~~ in a pharmaceutically effective amount with pharmaceutically acceptable diluents, carriers and/or adjuvants.

14. The method of claim 13 including the preparation of a recombinant attenuated pathogen comprising the steps:

- C Sub E51*
- a) inserting a nucleic acid molecule encoding a Helicobacter ^{immunogen} ~~antigen~~ into an attenuated pathogen, wherein a recombinant attenuated pathogen is obtained, which is capable of expressing said nucleic acid molecule or is capable to cause expression of said nucleic acid molecule in a target cell, and
 - b) cultivating said recombinant attenuated pathogen under suitable conditions.

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15. The method according to claim 14, wherein said nucleic acid molecule encoding a Helicobacter ^{immunogen} ~~antigen~~ is located on an extrachromosomal plasmid or inserted in the chromosome.

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16. A method for identifying Helicobacter ^{immunogens} ~~antigens~~, which raise a protective immune response in a mammalian host, comprising the steps of: *F*

- a) providing an expression gene bank of Helicobacter in an attenuated pathogen and
- b) screening the clones of the gene bank for their ability to confer protective immunity against a Helicobacter infection in a mammalian host.

Add C4

add E51 *add F'*

New Claims

1. Pharmaceutical composition comprising as an active agent an immunologically protective living vaccine which is a recombinant attenuated bacterium which comprises at least one heterologous nucleic acid molecule encoding a Helicobacter antigen, wherein said pathogen is capable of expressing said nucleic acid molecule or capable of causing the expression of said nucleic acid molecule in a target cell.

AMENDED SHEET